

CLAIM SUMMARY DOCUMENT:

Claims 1-20 (Canceled)

Claim 21 (Currently Amended) A method for sequencing a heterogeneous population of single stranded DNA molecules simultaneously and without spatial separation, wherein each DNA molecule is present in a unique amount and each DNA molecule bears a primer that provides a double stranded portion, which method comprises the following steps:

- a) contacting the plurality of single stranded DNA molecules with hybridization probes, each probe comprising a label cleavably attached to a known base sequence of predetermined length, the array containing all possible base sequences being incapable of ligation to each other, wherein the contacting is carried out in the presence of ligase under conditions to ligate to the double stranded portion of each DNA molecule, the probe bearing the base sequence complementary to the single stranded DNA molecule adjacent to the double stranded portion thereby to form an extended double stranded portion which is incapable of ligation to further probes; and
- b) removing all unligated probes; followed by the steps of:
- c) cleaving the ligated probes to release each label;
- d) recording the quantity of each label; and

- ⑤ activating the extended double stranded portion to enable ligation thereto; wherein
- ⑥ steps (a) to (e) are repeated in a cycle for a sufficient number of times to determine the sequence of each single stranded DNA molecule by determining the sequence of release of each label.

for sequencing DNA, which comprises:

- (a) obtaining a target DNA population comprising a heterogeneous population of single-stranded DNAs to be sequenced, each of which is immobilized in a unique amount in the same reaction zone and bears a primer to provide a double-stranded portion of the DNA for ligation thereto;
- (b) contacting the DNA population with an array of hybridization probes, each probe comprising a label cleavably attached to a known base sequence of predetermined length, the array containing all possible base sequences of that predetermined length and the base sequences being incapable of ligation to each other, wherein the contacting is carried out in the presence of ligase under conditions to ligate to the double-stranded portion of each DNA the probe bearing the base sequence complementary to the single-stranded DNA adjacent the double-stranded portion thereby to form an extended double stranded portion which is incapable of ligation to further probes; and

- (c) removing all unligated probes, followed by the steps of:
- (d) cleaving the ligated probes to release each label;
- (e) recording the quantity of each label, and
- (f) activating the extended double-stranded portion to enable ligation thereto;

wherein

- (g) steps (b) to (f) are repeated in a cycle for a sufficient number of times to determine the sequence of each single-stranded DNA by determining the sequence of

release of each label.

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Claim 22 (Original) A method according to claim 21, wherein the array comprises a plurality of sub-arrays which together contain all the possible base sequences, and wherein each sub-array is contacted with the DNA population according to step (b), unligated probes are removed according to step (c), and these steps are repeated in a cycle before step (d) so that all of the subarrays contact the DNA population.

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Claim 23 (Original) A method according to claim 21, wherein the target DNA population is obtained by sorting an initial DNA sample into sub-populations and selecting one of the subpopulations as the target DNA population.

A *3*
Claim 24 (Original) A method according to claim 23, wherein the initial DNA sample is cut into fragments, each having a sticky end of known length and unknown sequence, which fragments are sorted into sub-populations according to their sticky end sequence.

5 *1*
Claim 25 (Original) A method according to claim 24, wherein each single-stranded DNA is immobilized at one end.

6 *1*
Claim 26 (Original) A method according to claim 24, wherein the label of each probe comprises a mass label, and the quantity of each label is recorded according to step (e) using mass spectrometry after release of the label in step (d).

7 *1*
Claim 27 (Original) A method according to claim 24, wherein the known base sequence is blocked at its 3'OH.

8 *7*
Claim 28 (Original) A method according to claim 27, wherein the step (d) of cleaving the ligated probes to release each label unblocks the 3'-OH of the extended double-stranded portion according to step (f).

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Claim 29 (Original) A method according to claim 28, wherein the label of each probe
is cleavably attached to the 3'-OH of the base sequence.

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Claim 30 (Original) A method according to claim 21, wherein the base sequence of
each probe is unphosphorylated at both 3' and 5' ends and step (f) comprises
phosphorylating the 5'-OH of the extended double-stranded portion.

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Claim 31 (Original) A method according to claim 21, wherein the predetermined
length of the base sequence is from 2 to 6.

12 11
Claim 32 (Original) A method according to claim 31, wherein the predetermined
length of the base sequence is 4.

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Claim 33 (Previously Amended) A kit for sequencing a heterogeneous population of
DNA templates, each immobilized in a unique amount in the same reaction zone, which kit
comprises:

(a) an array of hybridization probes, each probe comprising a label cleavably
attached to a known base sequence of predetermined length, the array

containing all possible base sequences of that predetermined length and the base sequences being incapable of ligating to each other; and

(b) a means for resolving a measured quantity of a hybridized probe into quantities which correspond to unique amounts of the templates to which the probe hybridizes.

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Claim 34 (Original) A kit according to claim 33, wherein the known base sequence is blocked at its 3'-OH.

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Claim 35 (Original) A kit according to claim 34, wherein the label of each probe is cleavably attached to the 3'-OH of the base sequence to prevent ligation thereto.

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Claim 36 (Previously Amended) A kit according to claim 33, wherein the base sequence of each probe is unphosphorylated at both 3' and 5' ends.

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Claim 37 (Original) A kit according to claim 33, wherein the label of each probe comprises a mass label.

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Claim 38 (Original) A kit according to claim 33, wherein the predetermined length of
the base sequence is from 2 to 6.

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Claim 39 (Original) A kit according to claim 38, wherein the predetermined length of
the base sequence is 4.

Claim 40 (Canceled)

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Claim 41 (Previously Added) A method of using the kit of claim 33 comprising:
(a) contacting a target DNA population with the array of hybridization probes;
(b) cleaving the labels from hybridized probes to identify the hybridized probes;
and
(c) determining the sequence of the DNA from the identity of the hybridized probes.

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Claim 42 (Previously Added) A kit according to claim 33, wherein the means
comprises an algorithm.

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Claim 43 (Previously Added) A kit according to claim 33, wherein the means
comprises a computer program.

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